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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPS FORD, JANET L	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 12/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/719,870	DAMHA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,7-17,36 and 43-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,7-17,36 and 43-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

2. Applicant's amendment filed 9/18/2006 does not comply with 37 CFR 1.121(c), which requires

Amendments to the claims filed on or after July 30, 2003 must comply with 37 CFR 1.121(c)(2) which states:

(c) *Claims.* Amendments to a claim must be made by rewriting the entire claim with all changes (*e.g.*, additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(2) *When claim text with markings is required.* All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of "currently amended," and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of "currently amended," or "withdrawn" if also being amended, shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as "withdrawn-currently amended."

3. In the instant case, Applicants have amended claim 43 to recite dependency on claim 236, however there are no markings to indicate this change, and there is no status identifier to indicate that the claim is currently amended.

Claim Rejections - 35 USC § 102

4. The rejection of claims 2, 36, and 43-46 under 35 U.S.C. 102(a) as being anticipated by Wilds et al., is withdrawn in response to Applicant's amendment.

Claim Rejections - 35 USC § 102

5. Claims 2, 36, and 43-46 remain rejected under 35 U.S.C. 102(e) as being anticipated by Manoharan et al. (US Patent No. 6,369,209 B1), for the reasons of record.

6. Applicant's arguments filed 9-18-06 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that the instant application has a priority date of June 19, 1998. However, contrary to Applicant's assertions, the present amendment to the claims to recite "mixed base" does not have full support in the foreign priority document. The scope of the instant claims encompasses oligonucleotides consisting of any 2'-deoxy-2'-fluoro-β-D-arabinonucleobase, including 2'-deoxy-2'-fluoro-β-D-arabino-guanosine however the priority document provides only support for the synthesis of oligonucleotides consisting of a combination of 2'-F-araC, 2'-F-araA, or 2'-F-araT. The phrase "mixed base" encompasses any 2'-F-ara-nucleobase, however contrary to Applicant's assertions, the scope of the instant claims read beyond the scope of the foreign priority document,

which does not disclose oligonucleotide compounds consisting of mixed base 2'-F-ara-nucleobases, wherein said nucleobase includes guanosine.

Manoharan et al. disclose oligonucleotides that are disclosed as useful in therapeutic and investigative purposes. The oligonucleotides of this reference are also disclosed as having modifications that will increase affinity and nuclease resistances while concurrently serving as substrates for RNAse H when bound to a target RNA strand.

As stated in the prior Office Action, Example 67 of this reference describes the synthesis of 2'-fluoro-β-D-arabinofuranosyl oligonucleotides comprising a mixed base sequence, wherein one of the synthons used to design the oligonucleotides includes a protected 2'-F-ara-guanosine.

Claim Rejections - 35 USC § 103

7. Claims 2, 36 and 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheng et al. (US Patent No. 5,646,126) in view of Kois et al., McCormick, Giannaris et al., and Cook et al. (US Patent No. 5,623,065).

1) Cheng et al. describe oligonucleotides comprising 2'-deoxy, 2'-fluoro or 2'-difluoro nucleosides, wherein between 8 and 18 of said nucleosides are linked consecutively, see Figure 1, formula 2, see also claim 1. Specifically, the compounds of Cheng et al. encompasses wherein the R1 and R2 substituents of the 2' position of the nucleosides comprises either H or F, or wherein both R1 and R2 are F (fluorine) see col. 63, lines 24-25. Additionally, Cheng et al. teach that ODNs (oligonucleotides)

including α and β arabinosides, are included within the scope of the invention (col. 9, lines 33-39).

Cheng et al. does not specifically disclose isolated oligonucleotides comprising arabinose sugars and 2'-fluoro or 2'-difluoro modified nucleosides consecutively linked in the same molecule.

2) Kois et al. (SEE IDS of 5-15-2002, Nucleosides & Nucleotides, Vol. 12., No. 10., pages 1093-1109), and Kois et al. (SEE IDS of 5-15-2002, Nucleic acids Symposium Series, 1993, No. 29, pages 215-216.) disclose oligonucleotides that are uniformly modified with 2'-deoxy-2'-fluoro-β-D-arabinonucleotide modifications, see for example, Table 1, oligomers 5 and 6. The oligomers are disclosed in a 5μM solution in buffers A-C, absent evidence to the contrary, at least buffer B may serve as pharmaceutically acceptable carrier.

Kois et al. discloses nucleic acid compounds consisting of 2'-deoxy-2'-fluoro-β-D-arabinonucleotide modifications, however this reference does not disclose nucleic acid compounds comprising a mixed base sequence.

3) McCormick (US 4,760,017) discloses the use of β-D-arabinonucleosides in the synthesis of the arabinonucleic acid oligonucleotides, see Example 1. The arabinonucleic acid oligonucleotides consisting of mixed base β-arabinose sugars of McCormick are disclosed as capable of forming structures with complementary DNA or RNA, see col. 7, lines 5-26 of McCormick. Additionally, the hybridization solution containing the arabinonucleic acid probes described in col. 8, lines 1-18, can be

considered an acceptable carrier of the oligonucleotides consisting of β-arabinose sugars as recited in the instant claims.

McCormick does not disclose β-arabinose sugars comprising 2'-Fluoro modifications.

4) Giannaris et al. discloses oligoarabinonucleotides of mixed base composition (see Table 3). This reference teaches that oligoarabinonucleotides can be readily prepared by conventional solid-phase methodology employing phosphoramidite chemistry. Oligoarabinonucleotides were found to hybridize with complementary RNA and DNA exhibiting *Tm*'s comparable to, and in some cases greater than, the corresponding unmodified oligomers (see page 915). Giannaris et al. concluded by suggesting evaluating the effects of mixed base composition and 2'-modification on the ability of oligoarabinonucleotides to complex with both single and double stranded DNA and RNA (see page 915, 2nd col., 1st paragraph).

Giannaris et al. does not disclose β-arabinose sugars comprising 2'-Fluoro modifications.

5) Cook et al. (US Patent No. 5,623,065) discloses oligonucleotides comprising 2'-substiuents, in particular 2'-deoxy-2'-fluoro modified oligonucleotides are reported to increase the binding affinity of the substituted oligonucleotides, by 1.6 °C per substituted nucleotide unit of the oligonucleotide (col. 9, 3rd paragraph). Additionally, beta-nucleosides, and arabinofuranosyl nucleosides are also encompassed by the oligonucleotides of Cook et al. (col. 11, 3rd paragraph).

It would have been obvious to one of ordinary skill in the art at the time of filing to modify the oligonucleotides of Cheng et al. with the teachings of McCormick, Giannaris et al., Kois et al. and Cook et al. in the design of the compositions of the present invention. It would have been obvious to modify the oligonucleotides of Cheng et al. to comprise 2'-difluoro or 2'-fluoro β–arabinosyl nucleosides because, Cheng et al. expressly teach that their disclosed invention encompasses oligonucleotides comprising these modifications. Moreover, one of ordinary skill in the art seeking to enhance the properties of an oligonucleotide would have been motivated to modify the teachings of Cheng et al. to design the compounds of the present invention because Kois et al. (both references) teach that oligonucleotide stability can be increased by introducing 2'-deoxy-2'-β-D-fluoro-arabinofuranosyl nucleosides into the oligonucleotide structure. Moreover, it would have been obvious to modify the oligonucleotides of Chen et al. to comprise a mixed base structure, since Giannaris et al. clearly provide motivation for evaluating the effects of a mixed base structure in an oligoarabinonucleotide on it ability to form complexes with both snigle and double stranded nucleic acid structures. Furthermore, one of ordinary skill in the art would have been motivated to modify the structures of Chen et al. to comprise 2'-fluoro modification, since this substitution is disclosed in the prior art at functioning to increase the binding affinity of oligonucleotides comprising this modification. Moreover, 2'-fluoro-2'-deoxy-arabinofuranosyl modifications are well known in the art, see for example Kois et al. (both references). One of ordinary skill in the art would have had a reasonable expectation of success in designing the compounds according to the present invention comprising a mixed base

sequence, since Kois et al. (both references) describes the synthetic steps necessary for introducing 2'-deoxy-2'-fluoro-arabinofuranosyl moieties into an oligonucleotide structure. Moreover, the ordinary skilled artisan would have had a reasonable expectation of success for making a mixed base oligonucleotide, since Giannaris et al. and McCormick describe the synthesis of oligonucleotides comprising a mixed base arabinonucleotide sequence.

Therefore, the invention as a whole would have been *prima facie* obvious over Cheng et al. in view of McCormick, Giannaris et al., Kois et al. and Cook et al.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 43-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 (and those claims dependent therefrom) recite the phrase "Oligonucleotide according to claim 236," this phrase is vague and indefinite since there is no claim 236 presently pending in this application.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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